REMARKS

Reconsideration and withdrawal of the rejection as set forth in the Parent Application is respectfully requested in view of the foregoing amendments and the following remarks with respect to all the claims now in the application, namely claims 16 - 27.

It should be noted that enclosed herewith is a Declaration under 37 C.F.R. 1.132 by the inventor Birgit Helm which is provided with several of the references noted in the Declaration (Refs. 7-9)(as Exhibit A). Also enclosed is a curriculum vitae of the inventor (as Exhibit B) which clearly shows that this inventor is one of high skill in the field. Finally, some additional literature relating to the general field to which the invention pertains is also enclosed (Exhibits C-F).

Claims 16-24 stand rejected as being obvious over Cantor et al. in view of Gilfillan et al, and Levi-Schaffer et al. In addition, Claim 17 stands rejected as obvious over Wilson et al.; if this cannot be shown to be entitled to the priority date since Wilson is an intervening disclosure.

At the outset, it should be noted that the prior art and the present invention relate generally to the technology using certain cell lines which are secretor variants capable of binding human IgE as substitute for human FcϵRI as a model or assay tool;

using the tool to test the efficacy of anti allergen compounds by sensitizing the cells, exposing to allergen and compound and measuring binding of IgE or release of mediators.

Applicants do not dispute that these techniques are established tools for working with sensitizing cells and known allergies.

The Examiner accepts the novelty of claims on file, primarily by virtue of the absence of a sensitizing agent (human IgE).

Applicants have previously submitted that the present application relates to the use of "virgin" substances the allergenicity of which is not known and which is determined without the addition of IgE. Applicants submit with this response further illustration of the different assays which can be performed with the above known tools and the implications thereof, specifically in the form of recent publications by the inventors which employ the method of the invention as the prime assay tool, as distinct from known methods as disclosed in Gilfillan et al., Cantor et al. and Levi-Shaffer et al. The publications, which are filed after the priority date of this application serve merely as illustration, distinguishing the nature of the known and novel assay (determining potential allergens as opposed to studies with known allergens) and, moreover, illustrating the significance of that distinction.

Applicants respectfully submit that the distinction is so significant in terms of the usefulness of the method of the invention that not even with hindsight could the teachings of Cantor et al., Gilfillan et al. and Levi-Shaffer et al. be considered to render it obvious.

In the publications: "Assessment of molecular basis of pro-allergenic effects of cigarette smoke", Smyth et al., (Exhibit (C)) submitted for publication, illustrates the present invention in identifying pollutants in cigarette smoke which induce a mast cell response. In the examples RBL cells were exposed to cigarette smoke and mediator release determined. Nature and type of mediator release was observed and the results were used to study components in cigarette smoke responsible for potential immune modulatory activity, which can in turn be used to assist in elimination from tobacco or permit the assessment or development of potential antagonists. It is important that this study uses unsensitized cells since only by this means can the potential allergenicity of a substance be determined, and studied <u>without</u> distortion of results by sensitized response.

In "protein and cell engineering of components of the human IgE receptor/effector system; applications for therapy and diagnosis" <u>Technology and Health Care</u>, 6 (1998) 195-207 (Exhibit D) Helm et al. at 3.2 and particularly line 4 at page 203 the

distinction of the invention is clearly stated and explained. "In order to assess the technology (of the invention) we sensitized the cells with the serum of a bee-venom sensitive individual (EMC) and, following challenge with major bee-venom phosphlipase A_2 (PLA_2) we could, as expected demonstrate mediator release. Surprisingly, however, control experiments, were non-sensitized cells had been incubated with the same concentration of antigen in the absence of serum containing bee-venom specific IgE, cells also responded with the de-granulation of cellular mediators." The paper goes on to state that this discovery enable further studies to be carried out distinguishing active and inactive venom types. These observations were found to be applicable to a full range of occupational and environmental allergens. This information was then used to study the binding site mechanism and can be used to engineer anti-allergic drugs as variant forms of IgE and potential blocking agents of IgE receptor interacting and mast cell activation.

References 10 and 11 (Exhibits E and F respectively) cited in this latter publication are also enclosed. As discussed in the Declaration, these further illustrate the surprising nature of the finding of the invention referred to in the latter publication.

With respect to the Examiner's rejection of Claim 17, Claim 17 has been amended by deletion of "human IgE" and replacing

with "sensitizing agent", and Claim 17 as amended is clearly entitled to the priority date. At page 6, line 13 is disclosed the method of Claim 17 comprising exposing a mast cell line or basophil cell line in a defined manner. At line 13 is stated that by preference the mast cell line is a secretor variant of a RBL-2H3 cell-line which may or may not be transfected with a moiety capable of binding human IgE; note: moiety capable of binding IgE is a receptor = alpha - chain of the human high - affinity receptor = Fc ϵR1.

By implication therefore, the RBL-2H3 secretor variant transfected with the α-chain of the human high-affinity receptor is a subset of the mast cell line, and implicitly therefore disclosure of the mast cell-line includes disclosure of a transfected secretor variant.

Moreover, with reference to page 3, line 19 this is clearly stated..."In a preferred method... the mast cell line is an RBL-2H3 cell-line but in any case the cell-line is transfected with a molecule capable of binding human IgE. Alternatively the cell-line is a secretor variant and is of mast cell or basophil lineage and is transfected with a moiety capable of binding human IgE". It will be apparent from the accompanying Declaration that the invention differs from the prior art methods (including the method referred to at page 3) not by selection of cell-line but by manner

of its incubation and exposure. Accordingly, the claims of the invention properly encompass such a method irrespective of specific mast or basophil cell type. Thus, it will be appreciated, especially from the accompanying Declaration, that the invention is in no way limited in its potential application to the RBL-2H3 cell-line.

By this Amendment, new claims 26 and 27 have also been added which are entitled to the priority whereby Wilson is not available as prior art, or alternatively, are patentable over Wilson et al. Specifically, method claim 26 which is dependent on claim 16 defines the cell-line as being a secretor variant which may or may not be transfected with a moiety capable of binding human IgE (note: the receptor's alpha-chain binds human IgE). In addition, new claim 27 which is dependent on claim 17 specifically provides that the cell-line is exposed in the absence or presence of an allergen.

Support for changes to the claims and new claims can be found in the specification and claims. Specifically, the amendments to Claims 16 and 17 (secretor variant: a sensitizing agent) finds support in original Claims 16 and 17; the amendment to Claim 18, finds support at page 12, lines 10-13 of the specification; the amendment to Claim 21 finds support at page 13, line 23 of the application and Claim 26 is derived from Claim 16 as

amended ("the cell-line is a secretor variant which may or may not be transfected...") and Claim 17 ("the cell-line... is transfected..."); and Claim 25 finds support at page 19 and relates in particular to a known genetic assay technique, reverse transcriptase polymerase chain reaction.

Finally, it should be noted that Applicant has in fact, complied with 37 C.F.R. 1.808 as the statements pursuant to 37 C.F.R. 1.808 was provided with the Amendment in Reply to the First Office Action in the patent application.

In view of the foregoing, entry of the foregoing amendments and reconsideration and withdrawal of the rejection as set forth in the parent application are earnestly solicited.

Respectfully submitted,

Thomas M. Galgano
Registration No. 27,638
GALGANO & BURKE
Attorney for Applicant
300 Rabro Drive, Suite 135
Hauppauge, NY 11788
(516) 582-6161

TMG/jgg
Enclosures: Exhibits A-F
A:\PRELIMIN.AMD

I hereby certify that this correspondence is being deposited with the United States Postal Service as first-class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on January 19, 2000.

By: _____ Dated: January 19, 2000
Thomas M. Galgano, Esq.